Remarks

Claims 50-55, 70, 73, 82, 84-88, 91-94, 96-103, 110-114 and 119 are pending in the present application. Applicants herein amend claim 50 by incorporating claim 84 thereinto. Claims 84, 85, 86, 93 and 94 are cancelled herein. New claims 120 and 121 are supported by the present application, for example, in the paragraph bridging pages 8 and 9. Entry of the foregoing amendments is respectfully requested.

Information Disclosure Statements were properly filed in the present application on June 14, 2010 and July 16, 2010. Consideration is respectfully requested.

I. Background

The present invention (as amended herein) is directed to a seamless capsule comprising a polysaccharide gel membrane on the outer surface and optionally a coating on the gel membrane, wherein:

(i) the capsule encapsulates an emulsion comprising at least one oil, water and at least one emulsifier and the emulsion is an oil-in-water emulsion,

(ii) the oil is present in an amount of at least 50% by weight of the emulsion,

(iii) the polysaccharide gel membrane is an ionic gel membrane comprising at least one of alginate, propylene glycol alginate or pectin and the at least one of alginate, propylene glycol alginate or pectin is a salt of calcium, strontium, barium or aluminum,

(iv) the capsule is oblong, oval, or cylindrical,

(v) the capsule is enteric or delayed release, and

(vi) the emulsion does not contain marmelo mucilage.

The present invention is thus directed to the field of *seamless* capsules that are oblong, oval, or cylindrical, contain relatively large amounts of oil, and are enteric or delayed release.

II. At page 3 of the Office Action, the Examiner rejected claims 50-55, 70, 73, 82, 84, 87, 88, 91, 92, 96-99 and 110-112 under 35 USC § 103(a) as being unpatentable over Shigeno in view of Lee.

The Examiner's position is set forth in the Office Action and will not be repeated in detail here for purposes of brevity.

The Examiner argues that it would have been obvious to "incorporate the delayed or controlled release polymers of Lee within the capsules of Shigeno in order to yield an enteric or delayed release capsule…with a reasonable expectation of success because Lee teaches a microencapsulation method for the preparation of a controlled release oral drug delivery system and capsules, which utilize an enteric coating such as hydroxypropylmethylcellulose phthalate to obtain an enteric or delayed release capsule" (see the Office Action at page 6, first full paragraph).

Applicants respectfully traverse the foregoing rejection on the basis that the Examiner has not established a proper *prima facie* case of obviousness and respectfully request reconsideration thereof.

The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. See MPEP § 2143.02 I. Obviousness does not require absolute predictability, however, at least some degree of predictability is required. See MPEP § 2143.02 II.

Applicants respectfully submit that one skilled in the art would not have been motivated to combine the prior art references as proffered by the Examiner to arrive at the presently claimed invention with a reasonable expectation of success.

First, Shigeno is directed to macrocapsules and Lee is directed to microencapsulated drugs that exist in a freeze dried powdery matrix. There is nothing in the references to suggest

that the teachings from each reference can be combined as suggested by the Examiner with a reasonable expectation of success.

More specifically, Shigeno is directed to surfactant-containing seamless capsules having an inner layer and an outer layer, wherein the inner layer comprises an oily component and a surfactant. The capsules are produced using a triple nozzle or more and are indicated to be excellent in emulsive dispersibility (see Abstract and Figure 1). The capsules are soft capsules useful in pharmaceuticals and, for example, bath products (see the Abstract). The capsules that are disclosed in Shigeno are not microcapsules (as taught in Lee); i.e., they are soft capsules having a diameter of 0.2 mm to 2 cm (see col. 12, lines 42-44, and the Examples); indeed, Shigeno teaches that productivity increases "as the average particle diameter increases" (see col. 12, lines 46-47).

Lee is directed to a distinctly different freeze-dried matrix (than the capsules of Shigeno) that exists in a powdered state. More specifically, Lee discloses dispersing a drug in an oil, adding the oil to an aqueous phase containing a polysaccharide and emulsifier, emulsifying the two phases to form an oil-in-water emulsion containing drug-dispersed oil droplets having a diameter of from 1-5 microns, adding the emulsion to a multivalent cation-containing solution, and then freeze-drying the emulsion to obtain "a final product in powdery state" (see Lee at page 3, lines 38-39; emphasis added).

Lee teaches away from using its teachings in any delivery device other than a microencapsulated emulsion in a freeze dried matrix. Lee teaches throughout that it is the freeze dried powdered matrix containing the microencapsulated emulsion that is critical to achieving the targeted delayed release. For example, Lee states that "the microencapsulated emulsion is freeze dried to obtain a final product in powdery state which is the subject of the invention" (see page 3, lines 34-35; emphasis added).

As noted above, the Examiner argues that Lee demonstrates the use of enteric/delayed release polymers is "well-known in the capsule art" (see page 6 of the Office Action). However, as noted above, one reading Lee would conclude that it is the microencapsulated emulsion found in a freeze dried powdery matrix that is accomplishing the desired result in Lee. As a result, one skilled in the art would not conclude that the powdery matrix used in Lee to obtain the delayed release was optional as suggested by the Examiner. Indeed, such a modification of Lee (that freeze drying to form a powdered matrix was not critical) would clearly change the principle of operation of Lee. As stated in MPEP 2143.01 VI:

> If the proposed modification or combination of the prior art would change the principle of operation of the prior invention being modified, then the teachings of the references are not sufficient to render claims *prima facie* obvious.

Applicants respectfully submit that one skilled in the art would not have been motivated to combine the teachings of Shigeno (directed to macrocapsules) with Lee (directed to microencapsulated emulsions in a freeze dried powder matrix) with a reasonable expectation of success. The two systems are significantly different from one another and, as noted above, modifying the teachings from Lee as suggested by the Examiner would completely change the principle of operation of Lee.

Withdrawal of the foregoing rejection is requested on this basis.

Second, neither Shigeno nor Lee, alone or in any combination, teach or suggest the *seamless* capsules of the present invention that are "oblong, oval, or cylindrical."

That is, all the capsules disclosed and suggested by Shigeno are spherical, and the microencapsulated emulsions of Lee are also spherical (and subsequently freeze dried into a powdered state). There is no suggestion or motivation found in the references to modify such teachings and obtain capsules that are "oblong, oval, or cylindrical."

Nonetheless, at page 7 of the Office Action, the Examiner takes the position that "the particular shape of the capsule does not impart patentability to the instant invention, since the particular shape of the capsule would be based on personal preference in order to provide the for aesthetic appearance or for ease of consumability of the user."

However, the Examiner has not sufficiently explained or supported the view that the shape of a *seamless* capsule *having a large amount of oil* is a matter of mere "personal preference" in order to provide for aesthetic appearance or ease of consumability. (Indeed, contrary to the Examiner's position, none of the references actually cited by the Examiner throughout the Office Action in anyway teach *or suggest* their further modification from spherical capsules to the non-spherical capsules claimed herein.) Rejections on obviousness cannot be sustained by mere conclusory statements. See MPEP 2143.01 IV. Withdrawal of the rejection is requested on this basis.

Applicants respectfully submit that the present invention is unobvious and patentable over Shigeno in view of Lee. Accordingly, withdrawal of the foregoing rejection is respectfully requested.

III. At page 7 of the Office Action, claims 50-55, 70, 73, 82, 84, 87, 88, 91, 92, 96-102 and 110-112 are rejected under 35 USC § 103(a) as being unpatentable over Okamura in view of Gaserod and further in view of Lee.

Applicants respectfully traverse the foregoing rejection and respectfully request reconsideration thereof.

Okamura is directed to edible pearly capsules comprising a liquid drop comprising a water-soluble macromolecular substance at least a portion of which is marmelo mucilage, an oleaginous substance, and a water-soluble polyvalent metal salt (see claim 1). The edible

pearly capsules comprise a water-insoluble film formed from a water-soluble salt of alginic acid (see claim 1). In addition, the capsules made in Okamura are spherical.

Importantly, marmelo mucilage is a *required* feature of the teaching in Okamura; indeed, Okamura teaches that it is *critical* in order to make a suitable capsule.

For example, Okamura teaches that, "when it is attempted to entrap a large amount of an oleaginous substance in the capsule core, the integrity of the capsule as such cannot be maintained and the resulting limitation on the entrappable amount of the oleaginous substance has been a major obstacle to application of such capsules in the food industry" (see col. 1, lines 49-54).

Okamura's solution to this problem was to use marmelo mucilage in the stated process in amounts of "not less than 50 wt % and preferably as large as possible, for example not less than 60 weight %..." based on the weight of the water-soluble macromolecular substance (see col. 2, lines 27-32). Referring to the criticality of marmelo mucilage, Okamura states that the "water-soluble macromolecular substance at least a portion (generally not less than 50 weight %) of which is marmelo mucilage (a_1), the entrapping capacity of the oleaginous substance (a_2) will be *insufficient* if the proportion of marmelo mucilage is too small, while an excess of the mucilage would disrupt the balance of the composition" (see col. 3, lines 45-51; emphasis added). Okamura adds that the marmelo mucilage is an "essential component" (see col. 4, line 57). Moreover, the Examples in Okamura teach the criticality of using marmelo mucilage to encapsulate large amounts of oil (e.g., see the comparative testing set forth in Example 1).

The present invention expressly recites that the emulsion of the present claims does not contain marmelo mucilage. Since Okamura teaches that the presence of marmelo mucilage is required and critical, one skilled in the art would not have reasonably believed that marmelo mucilage could be excluded and still make capsules with a reasonable expectation of success.

Nothing in the secondary and/or tertiary references correct this deficiency.

The Examiner notes that the present claims recite the exclusion of marmelo mucilage, but takes the position that the present claims nonetheless recite "comprising" and therefore include the marmelo mucilage of Okamura. This position is not understood. It is respectfully submitted that the present claims expressly *exclude* marmelo mucilage and the use of the term "comprising" does not somehow change this.

In addition, in regard to claims 96 and 97, the Examiner relies on Gaserod as teaching that molecular weight of the alginate has an effect on both the release characteristics of an active ingredient as well as the strength of the capsules (referring to page 13, lines 18-29). However, the discussion in Gaserod relating to molecular weight (at page 13) relates to the chitosan, not the alginate.

With respect to the Examiner's reliance on Lee, Applicants refer the Examiner to the comments regarding Lee set forth above. One skilled in the art would not have been motivated to apply the teachings of Lee (directed to microencapsulated freeze dried powdered matrices) with the teachings of Okamura to arrive at the present invention with a reasonable expectation of success. To do so would change the principle of Lee. Accordingly, such a combination is not sufficient to render the present claims *prima facie* obvious. See MPEP 2143.01 VI above.

With respect to the shape of the presently claimed capsules, Applicants repeat the comments here as noted above.

In view of the foregoing, Applicants respectfully submit that the presently claimed invention is unobvious and patentable over the combination of prior art. Accordingly, withdrawal of the rejection is respectfully requested.

IV. At page 12 of the Office Action, the Examiner rejected claims 50-55, 70, 73, 82, 84, 87, 88, 91, 92, 96-102 and 110-112 under 35 USC § 103(a) as being unpatentable over Ueda in view of Gaserod and Lee.

Applicants respectfully traverse the foregoing rejection and request reconsideration thereof.

Ueda is directed to a method of preparing fish-egg-like edible products which are very similar to fish eggs such as salmon roe both in appearance and taste (see col. 1, lines 8-9). Ueda accomplishes this by preparing an emulsion comprising a viscous fluid consisting of an aqueous sol material and water, calcium salt, and an oil material, forming capsules by dropping the emulsion into an alginate solution and thereby surrounding the dropped emulsion with membranes of calcium alginate, and separating the encapsulated emulsion into the aqueous phase and the oil phase by heating (see col. 1, lines 59-67).

However, Ueda, alone or in any combination with Gaserod and Lee, does not disclose or suggest the criticality of the presently claimed seamless capsules comprising an oil-in-water ("O/W") emulsion.

Ueda broadly discloses the addition of the oil to the viscous fluid to obtain the emulsion (e.g., see col. 4, lines 1-2) and, in each of the Examples, the amount of the oil added to the viscous fluid is very small. There is no teaching or suggestion in Ueda about the criticality of the specific emulsion type in a seamless capsule containing large amounts of oil.

Applicants submit herewith a Declaration Under 37 CFR § 1.132 for the Examiner's consideration. As background, Applicants explain that their initial work centered on the water-in-oil ("W/O") emulsion due to the need of having high oil load in the emulsion and it was believed desirable to use the oil in the continuous phase of the emulsion. However, unexpectedly, Applicants have found that the O/W emulsion of the present invention has unexpected advantages over a W/O emulsion. For example, the O/W emulsion has been

found to provide a higher emulsion viscosity that offers important advantages in forming consistently shaped capsules as compared to W/O emulsions while using less calcium in the system and encapsulating larger amounts of oil.

In the attached Declaration, a side-by-side comparison between the two emulsion types was attempted in a process whereby the capsules were formed by dropping the emulsion into an alginate bath (similar in some respects to Ueda), but the W/O emulsion system struggled to make acceptable capsules while the O/W emulsion made very good capsules (see paragraphs II.D, II.E, and II.F of the Declaration). The low viscosity W/O emulsion did not break through the surface of the alginate bath and it formed a very irregular shaped matter before the gel started to form around it.[1] The ability of O/W emulsions to form stronger, more consistently shaped capsules suitable as dosage forms (using higher amounts of oil) than W/O emulsions is unexpected (see paragraph II.F. of the Declaration).

Moreover, the O/W emulsion unexpectedly makes acceptable capsules that are capable of encapsulating larger amounts of oil using less calcium *vis-à-vis* a W/O emulsion. Compare Examples 1 and 4 of the present application. The use of less calcium is very important because calcium needs to be removed by washing and it is highly desirable to use less if possible.

In addition, the ability of O/W emulsions to encapsulate larger amounts of oil than W/O emulsions is a distinct advantage, e.g., when the oil itself is an active or contains oil soluble actives.

The ability of O/W emulsions to form stronger, more consistently shaped capsules suitable as dosage forms (using less calcium and higher amounts of oil) than W/O emulsions is not suggested by any of the references (alone or in any combination).

[1] While this problem with the W/O capsule might be overcome by using additional components in the gelling bath such as sufficiently high levels of ethanol and a surfactant such as Tween 20 (e.g., see Example 1 of the present application), the use of such additional components is not preferred.

With respect to the shape of the presently claimed capsules, Applicants again repeat the comments here as noted above.

Finally, Applicants have herein added new claims 120 and 121 hereinabove. The Ueda invention clearly requires the use of a viscous fluid (as the aqueous phase) in the emulsion. The viscous fluid consists of locust bean gum, guar gum, xanthene gum, gelatin, carrageenan, and furcellaran in water (see col. 3, lines 17-22). New claims 120 and 121 specifically exclude the use of such polymers in the emulsion. Applicants respectfully submit that there is no disclosure or suggestion in Ueda NOT to use the polymers required therein in the aqueous phase. Indeed, since such materials are clearly required and are an important feature of Ueda, Ueda actually teaches away from claims 120 and 121 (excluding the use of such polymers).

In view of the foregoing, it is respectfully submitted that the presently claimed invention is unobvious and patentable over the prior art. Accordingly, withdrawal of the rejection is respectfully requested.

V. At page 18 of the Office Action, the Examiner provisionally rejected claims 50-55, 70, 82, 84, 87, 88, 91-92 and 110-112 on the ground of obviousness-type double patenting over claims 53-60 of copending USSN 11/713,176. Applicants will consider the desirability of filing a terminal disclaimer at such time as an indication of allowable subject matter is received. Applicants note that USSN 11/713,176 has now granted as US Patent No. 7,766,637 and a continuation application has been filed thereon (USSN 12/827,697).

Early favorably action is earnestly solicited.

Respectfully submitted,

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September 17, 2010

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